

**Amendment to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

Claims 1-68 (Cancelled)

69. (Currently amended) A method of screening for a modulator of Smurf activity which comprises detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound, wherein the Smurf activity detected is the activity of a Smurf comprising a WW domain and/or a HECT domain, and wherein the Smurf has an amino acid sequence similarity of ~~comprising~~ greater than 80% identity with the amino acid sequence depicted in SEQ ID NO:2.

70. (Previously presented) The method according to claim 69, wherein the Smurf activity is ubiquitination of a Smad polypeptide in a host cell.

71. (Previously presented) The method according to claim 69, wherein the Smurf activity is interaction of a Smurf WW domain with a PPXY domain of a Smad polypeptide.

72. (Previously presented) The method according to claim 71, wherein the test compound is screened for the ability to inhibit the interaction.

73. (Canceled)

74. (Canceled)

75. (Previously presented) The method according to claim 69, wherein the Smurf activity detected is the activity of a Smurf comprising the amino acid sequence depicted in SEQ ID NO:2.

76. (Cancelled)

77. (Previously presented) The method according to claim 69, wherein the Smurf activity detected is the activity of a Smurf comprising greater than 90% identity with the amino acid sequence depicted in SEQ ID NO:2.

78. (Previously presented) A method of screening for a modulator of Smurf activity which comprises detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound, wherein the Smurf activity detected is activity of the Smurf comprising the amino acid sequence depicted in SEQ ID NO:4.

79. (Cancelled)

80. (Cancelled)

81. (Previously presented) The method according to claim 78, wherein the Smurf activity is ubiquitination of a Smad polypeptide.

82. (Previously presented) The method according to claim 78, wherein the Smurf activity is ubiquitination of a Smad polypeptide in a host cell.

83. (Previously presented) The method according to claim 78, wherein the Smurf activity is interaction of a Smurf WW domain with a PPXY domain of a Smad polypeptide.

84. (Previously presented) The method according to claim 83, wherein the test compound is screened for the ability to inhibit the interaction.

85. (Previously presented) The method according to claim 78, wherein the Smurf activity is ubiquitination of a TGF $\beta$  receptor.

86. (Previously presented) The method according to claim 78, wherein the screening assay is conducted *in vitro*.

87. (Previously presented) The method according to claim 78, wherein the screening assay is conducted in a host cell.

88. (Previously presented) The method according to claim 69, wherein the Smurf activity is ubiquitination of a Smad polypeptide.

89. (Previously presented) The method according to claim 69, wherein the Smurf activity is ubiquitination of a TGF $\beta$  receptor.

90. (Previously presented) The method according to claim 69, wherein the screening assay is conducted *in vitro*.

91. (Previously presented) The method according to claim 69, wherein the screening assay is conducted in a host cell.

92. (Previously presented) A method of screening for a modulator of Smurf activity which comprises detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound, wherein the Smurf activity is ubiquitination of a Smad polypeptide.

93. (Previously presented) A method of screening for a modulator of Smurf activity which comprises detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound, wherein the Smurf activity is ubiquitination of a TGF $\beta$  receptor.

94. (Previously presented) The method according to claim 92, wherein the screening assay is conducted *in vitro*.

95. (Previously presented) The method according to claim 93, wherein the screening assay is conducted *in vitro*.

96. (Previously presented) The method according to claim 93, wherein the screening assay is conducted in a host cell.

97. (Previously presented) A method of screening for a modulator of Smurf activity which comprises detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound, wherein the Smurf activity is ubiquitination of a Smad polypeptide in a host cell.

98. (Previously presented) A method of screening for a modulator of Smurf activity which comprises detecting modulation of Smurf activity in the presence of a test compound relative to Smurf activity in the absence of the test compound, wherein the Smurf activity is interaction of a Smurf WW domain with a PPXY domain of a Smad polypeptide.

99. (Previously presented) The method according to claim 98, wherein the test compound is screened for the ability to inhibit the interaction.

100. (Previously presented) The method according to claim 98, wherein the screening assay is conducted *in vitro*.

101. (Previously presented) The method according to claim 98, wherein the screening assay is conducted in a host cell.

102. (Previously presented) The method according to claim 69, wherein the screening assay is conducted *in vivo*.

103. (Previously presented) The method according to claim 78, wherein the screening assay is conducted *in vivo*.

104. (Previously presented) The method according to claim 92, wherein the screening assay is conducted *in vivo*.

105. (Previously presented) The method according to claim 93, wherein the screening assay is conducted *in vivo*.

106. (Previously presented) The method according to claim 98, wherein the screening assay is conducted *in vivo*.